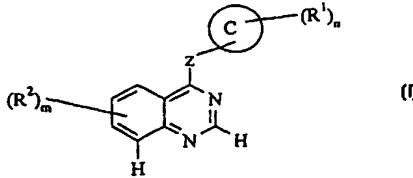


## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : <b>A61K 31/505, C07D 401/14, 413/14, 417/12, 405/12, 401/12</b>		A1	(11) International Publication Number: <b>WO 00/47212</b>	
			(11) International Publication Number: <b>WO 00/47212</b>	
(43) International Publication Date: 17 August 2000 (17.08.00)				
(21) International Application Number: PCT/GB00/00373			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 8 February 2000 (08.02.00)				
(30) Priority Data: 99400305.1 10 February 1999 (10.02.99) EP				
(71) Applicants (for all designated States except US): ASTRAZENECA UK LIMITED [GB/GB]; 15 Stanhope Gate, London W1Y 6LN (GB). ZENECA-PHARMA S.A. [FR/FR]; Le Galien, 1, rue des Chauffours, Boite postale 127, F-95022 Cergy Cedex (FR).				
(72) Inventors; and			Published	
(75) Inventors/Applicants (for US only): HENNEQUIN, Laurent, François, Andre [FR/FR]; Z.I. La Pompelle, Boite postale 1050, F-51689 Reims Cedex 2 (FR). PLE, Patrick [FR/FR]; Z.I. La Pompelle, Boite postale 1050, F-51689 Reims Cedex 2 (FR). STOKES, Elaine, Sophie, Elizabeth [GB/GB]; Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). MCKERRECHER, Darren [GB/GB]; Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).			With international search report.	
(74) Agent: BRYANT, Tracey; AstraZeneca, Global Intellectual Property, Patents, Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).				

## (54) Title: QUINAZOLINE DERIVATIVES AS ANGIOGENESIS INHIBITORS



## (57) Abstract

The invention relates to the use of compounds of formula (I), wherein ring C is an 8, 9, 10, 12 or 13-membered bicyclic or tricyclic moiety which optionally may contain 1-3 heteroatoms selected independently from O, N and S; Z is -O-, -NH-, -S-, -CH<sub>2</sub>- or a direct bond; n is 0-5; m is 0-3; R<sup>2</sup> represents hydrogen, hydroxy, halogeno, cyano, nitro, trifluoromethyl, C<sub>1</sub>-3alkyl, C<sub>1</sub>-3alkoxy, C<sub>1</sub>-3alkylsulphonyl, -NR<sup>3</sup>R<sup>4</sup> (wherein R<sup>3</sup> and R<sup>4</sup>, which may be the same or different, each represents hydrogen or C<sub>1</sub>-3alkyl), or R<sup>5</sup>X<sup>1</sup>- (wherein X<sup>1</sup> and R<sup>5</sup> are as defined herein; R<sup>1</sup> represents hydrogen, oxo, halogeno, hydroxy, C<sub>1</sub>-alkoxy, C<sub>1</sub>-4alkyl, C<sub>1</sub>-4alkoxymethyl, C<sub>1</sub>-4alkanoyl, C<sub>1</sub>-4haloalkyl, cyano, amino, C<sub>2</sub>-salkenyl, C<sub>2</sub>-salkynyl, C<sub>1</sub>-3alkanoyloxy, nitro, C<sub>1</sub>-4alkanoylamino, C<sub>1</sub>-4alkoxycarbonyl, C<sub>1</sub>-alkylsulphonyl, C<sub>1</sub>-4alkylsulphonyl, carbamoyl, N-C<sub>1</sub>-4alkylcarbamoyl, N,N-di(C<sub>1</sub>-4alkyl)carbamoyl, aminosulphonyl, N-C<sub>1</sub>-4alkylaminosulphonyl, N,N-di(C<sub>1</sub>-4alkyl)aminosulphonyl, N-(C<sub>1</sub>-4alkylsulphonyl)amino, N-(C<sub>1</sub>-4alkylsulphonyl)-N-(C<sub>1</sub>-4alkyl)amino, N,N-di(C<sub>1</sub>-4alkylsulphonyl)amino, a C<sub>3</sub>-7alkylene chain joined to two ring C carbon atoms, C<sub>1</sub>-4alkanoylaminoC<sub>1</sub>-4alkyl, carboxy or a group R<sup>56</sup>X<sup>10</sup> (wherein X<sup>10</sup> and R<sup>56</sup> are as defined herein); and salts thereof, in the manufacture of a medicament for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals, processes for the preparation of such compounds, pharmaceutical compositions containing a compound of formula (I) or a pharmaceutically acceptable salt thereof as active ingredient and compounds of formula (I). The compounds of formula (I) and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis.